UNITED STATES ARMY MEDICAL MATERIEL DEVELOPMENT ACTIVITY

FORT DETRICK, FREDERICK, MD 21701-5001

U.S. ARMY
MEDICAL MATERIEL DEVELOPMENT ACTIVITY

1989 ANNUAL REPORT

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION / AVAILABILITY OF REPORT Approved for Public Release; Distribution Unlimited
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION U.S. Army Medical Materiel Development Activity 6b. OFFICE SYMBOL (If applicable) SGRD-UMZ	7a. NAME OF MONITORING ORGANIZATION U.S. Army Medical Research and and Development Command
6c. ADDRESS (City, State, and ZIP Code) Fort Detrick Building T-622 Frederick, MD 21701-5009	7b. ADDRESS (City, State, and ZIP Code) Fort Detrick Building 504 Frederick, MD 21701-5012
8a. NAME OF FUNDING / SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command 8b. OFFICE SYMBOL (If applicable) SGRD-ZA	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick Building 504 Frederick, MD 21701-5012	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO.: See revs. PROJECT NO.: See revs. TASK NO.: See revs. WORK UNIT ACCESSION NO.: See revs.
11. TITLE (Include Security Classification) U.S. Army Medical Materiel Development Activity 1989 Annual Report (U)	
12. PERSONAL AUTHOR(S) CARL E. PEDERSEN, JR., Colonel, MS, Commanding	
13a. TYPE OF REPORT Annual Progress 13b. TIME COVERED FROM 1Jan89 TO 31Dec89	14. DATE OF REPORT (Year, Month, Day) 1990 January 31 15. PAGE COUNT
16. SUPPLEMENTARY NOTATION	
17. COSATI CODES FIELD / GROUP / SUB-GROUP	18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

This Annual Report, Calendar Year 1989, summarizes development projects monitored by the U.S. Army Medical Materiel Development Activity in projects authorized by The Surgeon General, the Army, and the Commander, U.S. Army Medical Research and Development Command, and supported by RDTE funds from the U.S. Army Medical Research and Development Command.

Keywords: X ray equipment; Computer aided tomography; Dental equipment; chemical warfare protective masks; laser irradiation protective spectacles; sterilizing equipment; vaccines; antiviral agents; drugs; (KT) ←

20. DISTRIBUTION / AVAILABILITY OF ABSTRACT ☐ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION
22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code) / 22c. OFFICE SYMBOL

DD Form 1473, JUN 86 — Previous editions are obsolete. — SECURITY CLASSIFICATION OF THIS PAGE UNCLASSIFIED

Block 10:

63807A	3M463807D808	AH	031
63807A	3M463807D808	BC	072
63807A	3M463807D8C9	AS	049
63807A	3M463807D993	BP	123
63807A	3M463807D808	BQ	077
64807A	3S464807D849	AB	024
64807A	3S464807D849	AW	023
64807A	3S464807D847	BA	011

U.S. ARMY MEDICAL MATERIEL DEVELOPMENT ACTIVITY
FORT DETRICK
FREDERICK, MARYLAND 21701-5009

31 JANUARY 1990

ANNUAL REPORT FOR PERIOD 1 JANUARY 1989 - 31 DECEMBER 1989

APPROVED FOR PUBLIC RELEASE
DISTRIBUTION UNLIMITED

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
FORT DETRICK
FREDERICK, MARYLAND 21701-5012

N O T I C E

DISCLAIMER

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

DISPOSITION

Destroy this report when it is no longer needed. Do not return it to the originator.

U.S. ARMY
MEDICAL MATERIEL DEVELOPMENT ACTIVITY

1989 ANNUAL REPORT

TABLE OF CONTENTS

INTRODUCTION

Calendar Year 1989 was marked by frenetic activity as the small staff of the U.S. Army Medical Materiel Development Activity kept pace with the many changes in development regulations and mobile funding profiles. Shepherding progress in each product under development by the three project management offices was never dull.

Accountability was the primary theme for our organization during the year. Intensive reviews and analyses, data base updates, a plethora of prioritization and concommitant funding alignments, MAMP and MSRC deliberations, IPRs, and high-level briefings to the senior AMEDD leadership and the DA/DOD staffs all served to reinforce the credibility of our efforts as well as acknowledge the fact that we actively serve the best interests of the user community.

Several high visibility materiel products are on track for fielding in the early 1990's, notably the major hardware items. The AMEDD program will clearly deemphasize the de novo development of medical materiel in the foreseeable future. Rather, modification of off-the-shelf items (NDI) will be the principal materiel development consideration in meeting AMEDD needs. Any perceived void, however, will be readily filled with products maturing from within the biologics and pharmaceutics side of the house. We have no shortage of requirements to substantiate our development program.

We are entering the final phase of our evaluation of the AMEDD acquisition system with a series of recommendations being prepared for the AMEDD leadership. If accepted, these will have profound implications on how the AMEDD acquisition process is conducted and how to best manage it.

In 1990, we intend to conduct thorough scrubs of our major support contracts which serve as the underpinnings for our products. It will become even more necessary to control cost growth in these areas as our development program resources continue to be scrutinized. Competition among product priorities will become even more keen, and product managers will be forced to use trade-offs which impact on cost drivers vis-a-vis need for product enhancements. "Better" may well become the worst enemy of "good enough."

The future looks both intriguing and challenging, and we stand ready to fully support the AMEDD community during an era of projected dynamic change.

CARL E. PEDERSEN, JR.
Colonel, MS
Commanding

THIS PAGE INTENTIONALLY LEFT BLANK

PROGRAM MANAGEMENT

INTRODUCTION

The Project Management Support Division (PMSD) provides centralized program-wide administrative, financial, contracting, and logistical support. Throughout 1989, the emphasis within PMSD has been on enhancing the support provided to the Project Management Divisions, and improving accountability for resources throughout the AMEDD materiel development spectrum.

MAJOR ACCOMPLISHMENTS

- 1989 Medical RDA MAMP: The FY89 Medical RDA Mission Area Materiel Plan (MAMP) Conference (March 1989) conducted product assessments for evaluating the USAMRDC Research, Development, and Acquisition (RDA) Program with respect to medical-related combat requirements. Representatives from USAMRDC, USAMMDA, USAMMA, Office of The Surgeon General (OTSG), U.S. Air Force, U.S. Navy, Academy of Health Sciences (AHS), and other Training and Doctrine Command (TRADOC) schools evaluated 139 products against 35 Medical Area capability issues (CI), and 11 medical-related Battlefield Development Plan (BDP) capability issues. AMEDD prioritization was developed and was approved by the Commanding General, USAMRDC and the Commandant, AHS. The increased participation by other AMEDD and non-AMEDD organizations, and other Services greatly enhanced conference effectiveness. As before, overnight turnaround on the team scoring resulted in very enlightening discussions in the final general session. Actions were initiated to incorporate the old AMEDD CI's into the Capability Packages of the Modernized Concept Based Requirements System (CBRS).

- Project Management Control System (PMCS): Contractor development of the Project Management Control System (PMCS) was completed in May 1989 with the revision of the Schedule Module. The revision resulted in the following enhancements: streamlined user interface, unified Oracle data management design, and capability to perform cross-schedule queries. The Work Breakdown Structure (WBS) code in the Schedule Module was standardized and mandatory command-level tasks to be included in R&A briefings were identified. Training on the Schedule Module and BPL was provided to USAMMDA personnel as required.

• General Analysis/Priority System (GAPS): The Resources Management Branch, with contractor support, developed and implemented GAPS, an automated resource management tool designed to assist in planning and programming the cost of product development. GAPS contains vital product identification and funding data concerning all products managed by USAMMDA. Phase I implementation of the system provides easy on-line access to all product data ("Z sheets") and a wide array of management reports which serve as invaluable tools in allocating limited dollar resources among competing products under development. Phase II, currently under development, will include an on-line Help Module as well as a Query Module to provide "what if" capabilities for the user. Phase II is scheduled to be completed by 3Q90.

• Automatic Data Processing Support: Additional software packages (such as BMDP Statistical Software, Turbo C, and Windows 286) increased specific user productivity. Macintosh SE's were introduced to more users to improve the quality of presentation graphics and provide a totally supportive environment for all users. With the conversion to Macintosh for graphics, and installation of a MAC II with a color monitor, color printer and scanner, USAMMDA is able to produce high-quality graphics output in-house; thereby eliminating the need to contract for such services. Work also began on installation of an ethernet local area network to speed data interchange.

• Program Development: USAMRDC experienced significant reductions in outyear program guidance during the 1989 Field Long Range Research, Development, and Acquisition Plan building process during spring and summer. USAMMDA, as the agent for preparation and defense of the development portion of the USAMRDC program, was heavily committed to preparing impact statements and program realignments to accommodate the reductions. Program reductions through FY95 averaged 15% then swelled to 48% from FY96 through FY06. Significant realignment in both research and development priorities will be required to adjust to Department of Defense RDA downsizing.

• Configuration Management Support: The Configuration Management Branch at the U.S. Army Belvoir Research, Development and Engineering Center (BRDEC), Fort Belvoir, VA, has been selected as the data repository for USAMMDA technical data packages (TDP) resulting from development contracts for products. This past year, the TDP for the Military Transportable Field Radiographic and Fluoroscopic System (MTFRFS) was delivered to BRDEC for reproduction and storage. Copies of these aperture cards will be provided to potential production contractors for the MTFRFS. Changes to the TDP resulting from the production of the systems will be made by government-approved engineering change proposals and provided to BRDEC for update of the TDP to maintain currency.

• Production Contract Preparation: The Logistics Management Branch was designated as the responsible office for preparing, staffing and coordinating the Army Acquisition Plan, statements of work for the production contracts for the PET Scope and the MTFRFS. Contract award is expected in mid-FY90.

• Major Support Contracts: The PMSD acts as the Contracting Officer's Representative for a major contract to provide approximately 25 technical manyears annually in support of the Project Manager's documentation requirements. The contract objective is to facilitate the timely and efficient execution of medical material development by providing a mechanism for preparing and assembling the support documentation necessary for coordinating and transitioning developmental medical products. To that end, 90 tasks were awarded during the year to provide 9 In Progress Review participant packages, either a System Concept and a Decision Coordinating Paper; 15 life cycle cost estimates; 13 integrated logistical support plans, 7 transition plans with Memorandum of Notification for each, 4 test and evaluation master plans, a logistics demonstration plan with contractor evaluation, a production readiness plan, a depot maintenance support plan, and a configuration management plan; 14 market investigations; several other incidental product-specific analyses and papers; as well as support for program-wide data collection and analysis efforts such as the General Analysis/Priority System and the Mission Area Materiel Plan. The support contract was awarded to Sherikon, Inc., in September based on a successful marketing presentation. The 90 tasks were split between 2 contractors, 54 to Engineering and Economics Research Inc., the exiting contractor, and 36 to Sherikon Inc., after award.

• Product Management Support: During the past year, the follow-on award for phase II of the development of the Field Medical Oxygen Generating and Distribution System (FMOGDS) was awarded and the Logistics Management Branch has been designated as the office to provide the contracting officer's technical representative for the contract. This resulted in arrangement of post contract award conferences, ILS Management Team meetings, Critical Design Reviews and various other meetings with the contractor and many outside Army agencies and offices. Several change orders to the contract have resulted, and the necessary modifications to the contract statement of work have been prepared and coordinated.

• Integrated Logistics Support and MANPRINT: As the responsible organizational element for managing all ILS and MANPRINT related actions, all necessary documentation to support these programs has been accomplished within the required milestone guidelines established for each product. These documents include ILS plans, review and coordination of MANPRINT management plans, preparation, staffing and coordination of ILS

plans, transition plans, System Support Packages, Basis of Issue Plan feeder data, and configuration management plans.

HUMAN RESOURCES

USAMMDA experienced an 80% turnover rate in clerical positions during 1989. Efforts are underway to standardize position requirements for secretaries among the Project Management Divisions and to establish promotion ladders to stabilize clerical support.

Through novel and intensive recruiting efforts, three hard-to-fill civilian specialties were committed: a Regulatory Affairs Specialist, a Pharmacologist, and a Toxicologist. Actions continue to resolve problems with recruiting and retaining civilian Logistics Management Specialists and military Logisticians.

- USAMMDA Key Personnel:

Position	Name	Date
Commander	COL C.E. Pedersen, Jr.	1 Jan 89 to 31 Dec 89
PM/AMSPMD	COL B.A. Schiefer	1 Jan 89 to 31 Dec 89
PM/BSPMD	Dr. W.E. Brandt	1 Jan 89 to 31 Dec 89
PM/PSPMD	COL R.O. Pick	1 Jan 89 to 31 Dec 89
Dir/PMSD	MAJ W.F. Heinemann	5 Sep 89 to 31 Dec 89
	LTC J.L. Chaffee	1 Jan 89 to 4 Sep 89

- USAMMDA Strength: As of 31 December 1989:

	Military	Civilian	Total
Required	25	51	76
Authorized	20	34	54
Actual	14	29	43

FISCAL PERFORMANCE

• **In-House**: USAMMDA in-house fiscal execution exceeded DA established targets for FY 89, and exceeded FY88 performance by 5% in obligations and 33% in disbursements. The improvement in disbursements was attributable to increased use of support contractor resources.

	Allotment	Obligations	Disbursements
FY 89 Dollars ($000)	3,799	3,770	2,478
Target (%)		94	49
Actual (%)		99	65

• **Program Wide**: Performance in the command-wide development program was not as successful as USAMMDA in-house, but much more successful than FY 88. Both laboratory and extramural program performance exceeded the obligation target. Critical disbursement targets were met in-house but not in the contract program although the total program performance increased by 70% over FY 88. Significant delays were encountered in applying contract modifications in two major projects (REFLUPS and DINS).

		PERCENT					
	Allotment	Laboratory		Extramural		Total	
Project	($000)	OBL	DISB	OBL	DISB	OBL	DISB
836	7,837	99	72	94	76	95	74
808	3,972	100	80	99	30	99	63
809	5,000	100	77	96	42	97	55
993	13,298	99	58	99	26	99	30
Total 6.3B	30,107	99	72	97	42	99	50
832	3,140	100	90	100	50	100	64
847	6,134	100	81	100	44	100	50
848	5,526	100	60	100	29	100	33
849	2,365	100	66	100	52	100	58
Total 6.4	17,265	100	76	100	40	100	48
Total Program	47,372	100	73	98	41	99	49

THIS PAGE INTENTIONALLY LEFT BLANK

APPLIED MEDICAL SYSTEMS
PROJECT MANAGEMENT DIVISION
THE PROGRAM

INTRODUCTION

The Applied Medical Systems Project Management Division is a multidisciplinary team with broad mission responsibilities to centrally manage the development and initial production of applied medical products, related diagnostic equipment, eyewear products, and pesticide delivery systems.

MILITARY RELEVANCE

Applied Medical Systems is committed to developing compact, lightweight, durable medical equipment to achieve both the Army's demanding Service-unique and multi-Service mission requirements. Diverse, multi-discipline technologies are integrated to create a wide range of state-of-the-art systems. Equipment initiatives are directed toward addressing medical defense against chemical warfare agents, medical protection against military hazards, and the ability to provide care to the combat casualty.

OBJECTIVES

Army readiness is predicated upon the timely and successful execution of programs by the Materiel Developer. To achieve this, Applied Medical Systems capitalizes on emerging Tech Base efforts and aggressively manages the development component of the AMEDD Research, Development and Acquisition process to meet DA and Joint Services performance and supportability requirements for field-survivable medical equipment.

PRODUCT DESCRIPTIONS

- The <u>High Capacity X-ray System</u> is a radiographic and fluoroscopic unit incorporating state-of-the-art solid state electronics, composite materials for lightweight construction, and mil-spec components for system reliability that complies with all radiation health and safety standards and meets the requirements for military operation.

- The <u>Field Medical Oxygen Generation and Distribution System (FMOGDS)</u> will provide both bedside and cylinder-refill oxygen capabilities within TOE hospitals and medical logistics organizations. The system is designed to reduce the logistics burden of acquiring medical grade oxygen.

- The Resuscitative Fluids Production and Reconstitution System (REFLUPS) produces sterile Water for Injection from a potable water source, combines that water with concentrated electrolytes to formulate parenteral solutions, and packages the solutions in sterile IV bags.

- Ballistic-Laser Protective Spectacles (B-LPS) afford ballistic protection against small mass (5.8 grain) low velocity (640-660 feet per second) fragments and directed energy protection against two wavelengths (ruby and neodymium) low energy (0.1-1.0 joule per pulse) lasers. Two versions are available, one clear and one tinted. An optional prescription lens carrier provides vision correction for the ametropic wearer.

- Laser Protective Eyewear (Materiel Change) is a family of polycarbonate eyewear which consists of the spectacle frontsert, helmet visor, spectacle lenses, mask outserts, and eyewrap. These eyewear products are designed to attenuate laser threats (three or more wavelengths) emitted from range finders, target designators, and low energy laser weapons.

- The Steam Vacuum Pulse Sterilizer System (SVPSS) is a microcomputer-controlled automatic steam sterilizer which employs a pressure/vacuum pulsing-conditioning principle for air removal and is designed to sterilize instruments, linens, and solutions for field hospitals.

- The Ethylene Oxide Sterilizer (EOS) is a stand-alone device for sterilizing non-heat sensitive devices as well as those sensitive to moisture or heat or those damaged by steam or liquid chemical sterilization. Products that fall into the latter categories include any plastic or rubber products such as catheters, resuscitation bags, anesthesia masks, surgical gloves, and most fiber optic instruments.

- The Special Operations Forces Sterilizer is a rugged, compact, lightweight, easy-to-use steam sterilizer for the Special Operations Forces medical personnel operating in mobile or unconventional warfare modes. This sterilizer can use electricity, wood fires, or gasoline/kerosene stoves as a heat source.

- The Field Computed Tomography Scanner is a compact x-ray scanning system which weighs about 1,600 pounds, requires less than ten kilowatts of power, can be deployed in a 1:1 ISO Shelter, produces diagnostic quality CT information, and because of the thermal management design, can be operated continuously.

- The **Filmless Digital Imaging Network System** is the combat casualty care incarnation of a battlefield filmless medical imaging network. The focus is on image acquisition, networking, display, and archiving for the echelon III and IV theater hospital environment. Peacetime variations of this technology are also being developed along two other basic thrusts; teleradiology and intra-hospital digital imaging networks.

- The **Miniature Dental X-Ray System (XRSDM)** is a small, lightweight, hand-held dental x-ray system for field use. The system consists of a hand-held x-ray generator subsystem (suitable for use with self-developing film or digital imager) and a digital imaging and storage subsystem for displaying images without the use of film.

- The **Powered Ventilator** is a lightweight portable device which uses an oxygen source or filtered ambient air to resuscitate and ventilate apneic casualties that are being medically evacuated. Ventilation can be administered through either an oropharyngeal mask or a cricothyroid cannula.

- The **Vital Signs Monitor (VSM)** is a noninvasive electronic device which will determine the heart rate and blood pressure of a casualty in chemical protective clothing while in a battlefield environment.

- The **Life Detector** is a hand-held device which provides a noninvasive method for detecting heart beat, respiration, or some other indicator of the presence of life, through chemical protective clothing without compromise to the protective ensemble or individual. It also determines the adequacy of prior antidotal treatment.

- **M-40 CB Protective Mask Vision Correction (Mainstream)** is a vision correction device which uses the M-17 wire optical insert with modified supporting hoops and is internally mounted on the M-40 CB protective mask. Prescription lenses are mounted in the frame component of this eyewear.

- **M-40 CB Protective Mask Vision Correction (Materiel Change)** is a vision correction device which uses the B-LPS prescription lens carrier and is internally mounted on the M-40 CB protective mask. Prescription lenses are mounted in the frame component of this eyewear.

- **M-17 and M-40 CB Protective Mask Laser Protective Outserts** are made of polycarbonate with applied absorptive dyes which afford laser eye protection from ruby and neodymium wavelengths. Additionally, the polycarbonate substrate serves to provide ballistic eye protection against small mass and low velocity fragments.

- The Optometry Field Set is made up of field operational optometric equipment which is composed of an examinee chair, instrument pole, examiner-examinee stools, supporting accessories, commercially available optometric instrumentation-equipment, and field chests.

- The Electronic Wet Bulb Globe Temperature Monitor (WBGT) will be available for use in field units to measure Dry Bulb Temperature (DBT), Wet Bulb Temperature (WBT), and Globe Temperature.

- The Hand-held, Heat-stress Calculator contains a prediction algorithm capable of computing work and rest cycles and associated water requirements for the individual soldier under a variety of environmental conditions.

- The Computer Assisted Post-Mortem Identification System (CAPMI) consists of computer hardware and a software routine that compares antemortem and postmortem dental records to yield a list of most probable matches for facilitating the process of identifying human remains.

- The Externally Mounted Rescue Hoist (EMRH) will be mounted on UH-60A (Black Hawk) Medical Evacuation (MEDEVAC) helicopters. It will allow 25 to 33 percent more space inside the aircraft compared to the current design with internally mounted rescue hoist. The additional cabin space can be used for patient care, medical equipment, and the MEDEVAC litter kit. Use of the EMRH will decrease mission time required for extraction of casualties or personnel and decrease aircraft weight.

- The Field Dental Operating and Treatment Unit (OTUDF) is a small, lightweight, mobile dental unit which will be used to provide emergency, limited preventive, and sustaining dental care in the field. It consists of a light source, suction apparatus, water reservoir, and high and low speed drills.

- The Decontaminable Folding Litter is capable of being decontaminated and providing a surface on which patients can be CWA decontaminated. It consists of aluminum poles and spreader bars, polypropylene mesh, retractable nylon handles, and ethylene-propylene-diene-monomer (EPDM) securing straps.

- The CW Resistant Field Dressing Cover consists of a strip of cotton gauze sandwiched between two laminates of polyethylene/nylon/polyethylene (PNP). The cover is used over the field battle dressing to protect open wounds and prevent penetration by chemical warfare agents.

- The CWA Protective Patient Wrap is a disposable fabric container to protect decontaminated or uncontaminated patients from chemical agents during evacuation in a field environment.

- The new **Field Medical Refrigerator** will replace the current refrigerator, used to contain blood and biologics, which has become logistically unsupportable.

- The **Individual Chemical Resuscitation Device (RDIC)** provides manually operated positive pressure respiratory resuscitation to assist in the restoration of normal breathing of a battlefield casualty. The RDIC filters chemical warfare agents from ambient air and is usable with an oropharyngeal mask or cricothyroid canula.

- The **Molecular Sieve Oxygen Generating System (MSOGS)** will be used for trauma and chemical agent patient resuscitation on Medical Evacuation (MEDEVAC) aircraft.

- The **High Capacity X-Ray (Materiel Change)** is a flywheel system which stores kinetic energy and produces short high power bursts of electrical energy to enable a high capacity x-ray to operate from a wide variety of power sources.

MAJOR ACCOMPLISHMENTS

- A validated Technical Data Package for the High Capacity X-Ray System was completed and procurement of 190 units was initiated.

- The Field Medical Oxygen Generation and Distribution System program continues on a dual track acquisition strategy (full scale development and a Nondevelopmental Item (NDI) approach). An Invitation for Bid (IFB) was advertised and awarded to MEPECC International for its Model M1-C Medical Oxygen and Air Generating System early in April 1989. Phase II of the Guild contract was also awarded in April 1989. The NDIs were delivered and accepted during August and Operational Testing was completed in November 1989.

- Deficiencies found during technical and user testing of the Resuscitative Fluids Production and Reconstitution System (REFLUPS) advanced development models were corrected this year. The new designs incorporated in the engineering development models significantly improve performance and reduce life cycle cost.

- Ballistic-Laser Protective Spectacles (B-LPS) were recommended for Type Classification - Limited Procurement (Urgent) by the Army Clothing and Equipment Board on 7 July 1989. Upon final approval by the Chief of Staff of the Army, follow-on procurement of product improved B-LPS will commence.

- **Two and three wavelength Laser Protective Visors** were approved for Type Classification - Limited Procurement (Urgent) by the SPH-4B Aviator Visor Type Classification Review Panel on 1 August 1989. Currently, there are 20,000 laser protective visors (10,000 two wavelength protection and 10,000 three wavelength protection) being procured for delivery to high priority aviation units.

- **The Steam Vacuum Pulse Sterilizer System (SVPSS)** was modified to include a variety of design enhancements to address RAM criteria. These changes were proven through Technical and Reliability Testing in mid-June 1989.

- Technical, reliability, and environmental testing of the Ethylene Oxide Sterilizer (EOS) was completed this year.

- The Imatron prototype Field Computed Tomography Scanner (CT) was tested at the factory on 26-27 February 1989. The device passed all tests specified in the contract.

- In January and February of 1989, a small size phosphor plate **Filmless Digital Imaging Network System** device was clinically tested at the Fort Meade and Fort Bragg community hospitals. The phosphor plate system was mated with the military high capacity x-ray device to produce the first military diagnostic quality digital x-ray image. In March, the DOD health Council approved a teleradiology system for Fort Meade and its surrounding clinics on the basis of specifications developed through the DINS project. This is the first tangible "technology transition" resulting from the DINS project. In May 1989, a teleradiology trial was conducted for the 18th MEDCOM in South Korea. Teleradiology images were moved between Osan AFB and the 121st Evacuation hospital in Seoul and from Georgetown University hospital in Washington, DC, across the Pacific to Seoul. In July 1989, a Filmless Digital Imaging System underwent a weeklong test at the Camp Bullis DEPMEDS site. This was the first operation of such a network under field conditions. No failures were experienced. In August, an In-Process Review (IPR) was chaired by MG Major, CG at HSC, to examine implementation of DINS at the new Madigan Army Medical Center. Issues from the IPR are under review within the AMEDD.

- **The delivery of prototype units for the Miniature Dental X-Ray System** was completed this year. A CEP test was conducted 14-25 August 1989.

- **The Powered Ventilator** Draft JSOR was revised and staffed for final review and comment in 4Q89. Modified Non-Developmental Item ventilators were procured for Echelons I/II and III/IV medical care and were tested in a Concept Evaluation Program (CEP) test 4-15 December 1989.

- Commercially available, Non-Developmental Item Vital Signs Monitors (VSM) identified within the Market Investigation were obtained by the government for testing. A CEP test was conducted 11-22 September 1989 by the U.S. Army Medical Department Board (USAMEDDBD). A Technical Test involving determination of vital signs using these devices on human subjects in a high noise and high vibration environment was conducted by the U.S. Army Aeromedical Research Laboratory (USAARL) in October 1989.

- Flash Reflectance Oximeter (FRO) and Personal Monitor and Communicator (PMC) prototypes for the Life Detector program were delivered this year.

- Production of 75,000 M-40 CB Protective Mask Vision Corrections (Mainstream) was completed on 18 April 1989. These mask vision correction frames were shipped to Army depots at Mechanicsburg, PA and Tracy, CA for requisitioning by the military optical fabrication laboratories.

- Fabrication of Optometry Field Sets was completed on 6 October 1989. Tobyhanna Army Depot, PA, received these field sets for initial staging of fabricated items with standard Army items.

- The Computer-Assisted Postmortem Identification System (CAPMI) Mission Element Needs Statement (MENS) was certified by TRADOC and is awaiting HQDA approval. Defense Eligibility Enrollment Reporting System (DEERS) Support Office (DSO) agreed to conduct a Pilot Study to verify the feasibility of incorporating the CAPMI antemortem dental data base into DEERS.

- The concept of an Externally Mounted Rescue Hoist (EMRH) was technically tested by the U.S. Army Aeromedical Research Laboratory (USAARL) during July-November 1989. Test results are pending.

- A correspondence IPR transitioned the Field Dental Operating and Treatment Unit (OTUDF) to USAMMA 30 January 1989.

- The National Stock Number 6530-01-290-9964 was assigned to the Decontaminable Folding Litter on 25 January 1989. A contract was awarded on 14 August 1989 to the National Industries for the Blind to conduct a Low Rate Initial Production.

- The Defense Personnel Support Center began formal acquisition procedures for the Field Medical Refrigerator in 4Q89.

- A Milestone Ia In-Process Review (IPR) was held for the Resuscitation Device, Individual, Chemical (RDIC) on 13 April 1989. It was determined that additional prototypes should be procured to incorporate the C2 canister filter into the design and to remove the PEEP valve. Prototypes were redesigned and tested at the Uniformed Services University of Health Sciences (USUHS) against soman poisoned swine.

- A Joint Working Group finalized the O&O Plan for the Molecular Sieve Oxygen Generating System (MSOGS) on 24 January 1989.

PROJECTIONS

- Procurement of the High Capacity X-Ray System will start early in 1990.

- Developmental testing of the Field Medical Oxygen Generation and Distribution System (FMOGDS) will begin April 1990 and Operational Testing of the developmental item beginning February 1991.

- The Resusitative Fluids Production and Reconstitution System (REFLUPS) will move into the Full Scale Development Phase in March 1990. Life Cycle Cost estimates, determined from the Abbreviated Analysis, which are driven by the process consumables will be substantially reduced.

- The Steam Vacuum Pulse Sterilizer System (SVPSS) contract is in its final year with delivery of the Technical Data Package expected 2Q90. The SVPSS contract will end in March 1990 following support of the IOT&E II. A Milestone III IPR will be held in 4Q90.

- The Ethylene Oxide Sterilizer System (EOSS) prototypes and a complete Technical Data Package for this effort will be delivered in 2Q90. A Milestone III IPR will be held in 3Q90.

- Procurement of the Special Operations Forces Sterilizer (SOF) will start in 1Q90.

- Clinical and technical tests for the Field Computed Tomography Scanner will begin in April of 1990. These tests will culminate in December 1990 prior to CEP testing which is anticipated in January 1991.

- Field trials will continue in 1990 for the Filmless Digital Imaging System (FDIS). A MS I/II will be held in 3Q90 to sustain a modified NDI approach. Teleradiology systems will be acquired for Fort Meade and Korea. DINS will be acquired for the new Madigan Army Medical Center.

- The Miniature Dental X-Ray System (XRSDM) developmental testing will be completed 1QFY90. A Milestone I/II IPR will be conducted in early February 1990.

- After receiving the test report from the CEP testing, a Milestone II Powered Ventilator IPR will be held in 2Q90.

- After receiving the Vital Signs Monitor CEP test report and Independent Evaluation Report, a Milestone II IPR will be held in early 2Q90 to decide if a Non-Developmental Item exists that satisfies the Tri-Services' needs.

- A CEP test will be conducted in mid-2Q90 on the Personal Monitor and Communicator and Flash Reflectance Oximeter prototypes of the Life Detector project.

- Engineering development prototypes for the M-40 CB Protective Mask Vision Correction (Materiel Change) will undergo technical and operational tests in 4Q90.

- Advanced development prototypes for the M-40 and M-17 CB Protective Mask Laser Protective Outserts will undergo limited user testing in 4Q90-1Q91.

- Fielding of the Optometry Field Set will commence 2Q90.

- The Pilot Study for determining the feasibility of incorporating the Computer-Assisted Postmortem Identification (CAPMI) dental data base into the Defense Eligibility Enrollment Reporting System will be conducted 2Q90.

- A Milestone I IPR will be held for the Externally Mounted Rescue Hoist in 2Q90, and decisions will be made regarding an NDI or a developmental effort strategy.

- The Defense Personnel Support Center will award a contract to purchase the new Field Medical Refrigerators in 3Q90.

- A Milestone II/III IPR will be held for the Individual Chemical Resuscitation Device (RDIC) in 2Q90.

- Delivery of off-the-shelf candidates for the Molecular Sieve Oxygen Generating System will occur in October 1990. Technical testing will begin in December.

- The High Capacity X-Ray (Materiel Change) prototypes being developed by the US Army Biomedical Research and Development Laboratory will be delivered for technical testing in December 1990.

THIS PAGE INTENTIONALLY LEFT BLANK

BIOLOGICAL SYSTEMS
PROJECT MANAGEMENT DIVISION
THE PROGRAM

INTRODUCTION

The Biological Systems Project Management Division manages the development and acquisition of biological products to prevent casualties or loss of soldier effectiveness due to disease. These diseases may be naturally acquired (close contact, unsanitary conditions, contaminated environment, biting insects), or acquired by deliberate exposure to aerosols. Product Managers exploit domestic and foreign medical technology to remedy deficiencies identified by the Combat Developer and monitor research projects for their application to disease protective measures.

MILITARY RELEVANCE

Casualties from disease have been a major cause of hospital admissions and ineffectiveness on the battlefield. Figures for admission for soldiers during a year in Vietnam were as follows: disease - 70.6 percent; battle casualty - 15.6 percent; nonbattle injury - 13.8 percent. Efforts to reduce the impact of disease on operations will make a significant contribution to soldier effectiveness.

OBJECTIVES

This Division's directive is to develop effective preventive measures against diarrheal diseases; malaria; acute respiratory diseases; hepatitis; insect-transmitted diseases such as dengue and Japanese encephalitis; hemorrhagic fevers and other diseases spread by aerosol (and rapid methods to identify the cause of illness); schistosomiasis; meningococcal disease; and opportunistic wound infections. Methods to address these deficiencies (some of which include treatment) are vaccines, immune enhancers, adjuvants, immune globulins, antiviral drugs, insect repellents, and rapid identification kits for clinical specimens.

PRODUCT DESCRIPTIONS

- <u>Salk Vaccine Production Facility</u> is a manufacturing facility dedicated exclusively to the production of vaccines and diagnostic reagents under Federal regulatory guidelines. The facility is managed by a task order contract for scheduling production of vaccines and reagents.

- University of Maryland Vaccine Testing Facility is used for evaluating vaccines in human safety and efficacy trials. The trials are done either in the 32-bed isolation ward or on an outpatient basis. Each trial is performed under a specific task order, with detailed protocols.

- Oxygen-Carrying Blood Expander is a resuscitative fluid for use in field medical units. Modified hemoglobin solutions are currently under development in the commercial sector. The Army plans to evaluate these products to determine suitability for military use.

- Rapid Identification System for Biological Agents is a portable, rugged, easily operated system designed to identify biological agents in clinical materials. In the test, drops of serum from soldiers exhibiting symptoms of disease are placed on credit card sized blotters in plastic holders. After the reagents are added and absorbed, positive or negative results are visible to the unaided eye in less than 30 minutes.

- Ribavirin is an antiviral drug that has been tested for efficacy against Hemorrhagic and Sandfly Fevers. The Army is evaluating the clinical studies that will be a part of a New Drug Application (NDA). The intravenous formulation could be used by military physicians to treat diseases such as Korean Hemorrhagic Fever and Lassa Fever.

- J-5 Human Monoclonal Antibody is secreted by cultured hybridomas that were created by fusing myeloma cells with cells from the spleen of a donor immunized with killed E. coli strain J-5. The collaborative effort between Walter Reed Army Institute of Research (WRAIR) and Centocor has shown that the monoclonal antibody, which reacts with the highly conserved lipid A region of the lipopolysaccharide, binds to a wide variety of endotoxins and to gram negative bacteria of many genera.

- Klebsiella/Pseudomonas Human Immune Globulins will treat opportunistic infections in burn and wound patients. The immune globulins will be obtained from the plasma of volunteers immunized with Klebsiella and Pseudomonas vaccines. Each vaccine contains antigens from multiple serotypes of the organism and was shown to induce antibodies in volunteer studies involving a collaborative effort between WRAIR and the Swiss Serum and Vaccine Institute (SSVI).

- Lassa Fever Immune Plasma is an immune globulin used to treat Lassa fever infections. The collection of human immune plasma in Africa is an ongoing contract effort. USAMRIID performs laboratory tests and selects the plasma units with sufficient antibody titers for fractionation into immune globulin.

• Hepatitis A Vaccine was produced at WRAIR by growing the virus first in cultured monkey kidney cells and then in human lung cells until antigen concentrations reached a stationary level. The virus was inactivated with formalin, safety tested according to regulatory guidelines, and tested in volunteers. Several inactivated vaccines, including a Smith, Kline and Beckman vaccine, will be tested in order to obtain the most immunogenic product.

• Adenovirus Vectored Hepatitis B Vaccine was developed by Wyeth Laboratories by using recombinant DNA technology to incorporate the Hepatitis B surface antigen gene into Adenovirus Type 7. This bioengineered adenovirus produces both Hepatitis B and Adenovirus 7 antigens in infected cell culture and has passed regulatory safety tests. The Army will test the vaccine in volunteers and use it in recruits if it can be licensed.

• Dengue Type 4 Live Vaccine is a non-disease producing strain of dengue 4 virus developed at WRAIR by growing the virus in cultured primary dog kidney cells and then in fetal rhesus monkey lung cells. The cell culture supernatant contains the attenuated virus which was lyophilized for long-term storage and shown to pass regulatory safety tests. After satisfactory human studies, the live vaccine will be combined with live vaccines for the other dengue virus serotypes.

• Rift Valley Fever Vaccine is prepared by growing the virus in cultured monkey lung cells at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and the Salk Institute, inactivating the virus with formalin, and storing it as a lyophilized product. This investigational vaccine has been used in at-risk laboratory workers, United Nations peace-keeping forces, and State Department mission personnel. Licensure of the vaccine will be considered when new production runs are required to replace current stocks.

• Vaccinia Vectored Venezuelan Equine Encephalitis Vaccine (VEE) will be produced by inserting into a live vaccinia virus carrier the VEE genes that direct the production of immunizing VEE antigens. This vaccine, which should elicit antibodies against both smallpox and VEE, is being developed under contract by the Centers for Disease Control (CDC) to replace a live VEE vaccine that is reactogenic in 15 percent of recipients. It will be a contingency vaccine for biological defense.

• Vaccinia-Vectored Korean Hemorrhagic Fever (KHF) Vaccine will be produced by inserting the KHF gene that controls the production of immunogenic KHF antigens into a live vaccinia virus carrier (smallpox vaccine). The resulting recombinant vaccine should elicit antibodies against both smallpox and KHF. This

vaccine, currently in the early stages of development, is being prepared in a collaborative effort between USAMRIID and the Salk Institute.

- Smallpox Live Vaccine is a new cell culture produced animal pox virus (vaccinia) that will be free of bacteria presently found in the calf lymph vaccine. This should allow intramuscular rather than percutaneous administration.

- Argentine Hemorrhagic Fever Live Vaccine (AHF) is a live, attenuated vaccine for military personnel being deployed to endemic or potential threat areas with this agent. The vaccine was prepared by growing the virus in fetal rhesus monkey lung cells in a collaborative effort between USAMRIID and the Salk Institute. Following successful efficacy studies in Argentina, a license application will be prepared.

- Japanese Encephalitis Vaccine is extracted and purified from infected mouse tissue by a Japanese company (Biken), and has been shown to reduce the incidence of disease in endemic regions of the world. It is currently being administered as an investigational vaccine since it is not licensed in this country.

- Chikungunya Live Vaccine is a live attenuated virus vaccine obtained by growing the virus in cultured human lung cells at USAMRIID. The Salk Institute produced the experimental lots under regulatory guidelines for testing in humans and, following additional human testing, it will be stored in a lyophilized form as a contingency vaccine.

- Falciparum Malaria Sporozoite Vaccine is a product of recombinant DNA technology and consists of the circumsporozoite protein of Plasmodium falciparum. The vaccine is produced under a no-cost agreement with Smith, Kline and French Laboratories. The vaccine is being tested in combination with different types of adjuvants in order to increase the antibody titers in volunteers.

- Vivax Malaria Sporozoite Vaccine is a product of recombinant DNA technology and consists of the circumsporozoite protein of Plasmodium vivax. The vaccine is following the development of the falciparum malaria vaccine by collaboration between WRAIR and Smith, Kline and French Laboratories; the most effective adjuvant for the falciparum vaccine will be given priority for the vivax vaccine.

- Q Fever Vaccine (Chloroform-Methanol Residue (CMR)) is a formalin inactivated vaccine prepared at the Salk Institute from rickettsia that are grown in embryonated eggs. The extraction with chloroform-methanol was devised at the USAMRIID and was

shown to eliminate severe skin reactions seen in animals inoculated with earlier vaccine. The vaccine is for biological defense.

- Tularemia Live Vaccine is a live, attenuated vaccine for military personnel being deployed to an area where there is a potential threat use of Francisella tularensis. New lots of vaccine have been prepared at the Salk Institute under slightly modified production protocols, and are currently being tested for safety in volunteers at USAMRIID. There may be sufficient efficacy data for licensure.

- Botulinal Toxoids, Types F & G, will be used in a polyvalent product for military personnel being deployed to an area where there is a potential threat use of Clostridium, botulinum toxin. The toxins will be purified from cultures of the bacteria that produce either Types F or G toxin, inactivated with formalin to produce the toxoid, and tested separately and then together for their ability to produce toxin neutralizing antibodies in humans.

- Shigella Vaccines are oral products containing live bacteria with specific antigens to protect against diarrheal diseases. These bioengineered vaccines are produced at WRAIR and tested at the University of Maryland Vaccine Testing Facility.

- N. meningitidis (Group B) Vaccine is a protein-based vaccine for use in conjunction with licensed polysaccharide vaccines to protect military personnel against epidemic cerebrospinal meningitis. The vaccine is a bacterial sub-capsular protein complexed to polysaccharide antigens. The product is a collaborative effort between WRAIR and Connaught Laboratories, and is necessary to protect soldiers against a larger number of strains of this organism.

- Schistosome Topical Antipenetrant is a niclosamide-based lotion originally designed at WRAIR and then formulated for application to human skin by Miles Laboratory. The niclosamide lotion prevents the penetration of free swimming schistosomal larva.

- Insect/Arthropod Repellant, Clothing Impregnant is a chemical treatment of permethrin to the Battle Dress Uniform to provide protection of the covered areas from insect/arthropod bites. One treatment lasts for the entire life of the uniform. Reports on permethrin toxicology, risk benefit analysis, and risk assessment have been prepared. These are components of a registration application to the Environmental Protection Agency (EPA) for a Military Use Only label.

• Insect/Arthropod Repellent Lotion (Materiel Change) is an improved, controlled release, topically applied insect repellent designed to provide protection from a broader spectrum of disease vectors and pests, especially biting midges. This recently approved effort will initially focus on selection of the best candidate repellent formulation for efficacy.

• Body Louse Toxicant is a powder formulation of malathion which will replace lindane as the standard pediculicide. Technical tests were completed on a commercially available preparation and showed the need to add an anti-caking agent to permit compatibility with mass delousing equipment. The procurement specification is being revised to incorporate the change.

MAJOR ACCOMPLISHMENTS

• A pilot lot of inactivated Hepatitis A Vaccine was produced at the Salk Vaccine Production Facility. A master seed of vaccinia virus containing a removable marker gene (in a position where genes coding for desired antigens could be inserted) was produced under regulatory guidelines for production of recombinant live vectored vaccines. Completion of Q Fever Vaccine preclinical testing showed that the new purified and inactivated product is nonreactogenic in animals, that it passed all safety tests, and that it is ready for testing in humans. A master and production seed was made for a new bacteria-free smallpox vaccine. A pilot lot was also made of a new candidate live attenuated Rift Valley Fever (RVF) Vaccine. Over 20 lots of inactivated RVF vaccine that had lost vacuum were pooled, filtered, and repackaged in 3 lots. The Johns Hopkins subcontractor tested the ability of Pseudomonas Exotoxin A to enhance Malaria Vaccine immunogenicity and found a fivefold increase in antibody titers. The first liposome vaccine (containing recombinant malaria sporozoite antigen) was also started in clinical trials.

• During this year, the University of Maryland Vaccine Testing Facility completed a study comparing simultaneous administration of Klebsiella and Pseudomonas vaccines with an alternate immunization schedule where the two vaccines were given at a 2-week interval. Both schedules produced similar results in titers in groups of 20 volunteers. Another study evaluated immunogenicity and safety of a Vi+ Ty21a Typhoid Vaccine. Only low responses were seen to the Vi antigen when volunteers were given one dose of vaccine ($1x10^9$). Additional work will evaluate titers in volunteers given three doses. Another task conducted this year was designed to evaluate safety of a candidate Shigella Vaccine derived by a mutation in the aromatic amino acid synthesis pathway. Finally, the Adenovirus Vectored Hepatitis B Vaccine was tested for safety and transmissibility.

- Army intention to test commerical Oxygen Carrying Blood Expanders advertised in Commerce Business Daily.

- Three companies submitted kits for the Rapid Identification System capable of detecting plague antigen in less than 30 minutes. Acquisition of 1000 kits for each of 4 agents from the 3 companies is in progress.

- The clinical section of an NDA for Ribavirin describing the field trials has been drafted.

- Five military medical centers are participating in clinical trials of the J-5 human Monoclonal Antibody. Volunteers with clinically diagnosed gram negative septic shock have been enrolled in the treatment protocol.

- A Request for Proposal (RFP) has been issued to obtain immune plasma to prepare Klebsiella/Pseudomonas Immune Globulins from volunteers immunized with both vaccines simultaneously.

- A Phase 2 study was initiated at Fort Campbell, KY, with Smith, Kline and Beckman's Hepatitis A Vaccine.

- Adenovirus Vectored Hepatitis B Vaccine IND Application was filed with the FDA in April 1989 by Wyeth Laboratories under a Cooperative Research and Development Agreement with the U.S. Army Medical Research and Development Command (USAMRDC). On 12 October 1989, the initial human safety study was initiated whereby three volunteers received the vaccine and three a placebo at the University of Maryland.

- A Milestone III In-Process Review (IPR) in June 1989 transitioned Rift Valley Fever Vaccine, as well as the three Equine Encephalitis Vaccines (Eastern, Western, and Venezuelan), from development to the Office of The Surgeon General. These vaccines are now on contingency deployment status.

- Horses vaccinated with recombinant Vaccinia Vectored VEE Vaccine virus developed virus-specific antibodies and were capable of surviving challenge with virulent virus.

- At USAMRIID, the gene coding for the two surface antigens of Korean Hemorrhagic Fever virus has been experimentally inserted into the DNA of the smallpox vaccine virus (vaccinia) antecedent to production of the Vaccinia-Vectored KHF Vaccine. Concurrently, the Salk Institute is preparing a certified vaccinia seed virus in cell culture to receive the antigen genes for vaccine production.

- The master and production seed lots of a new cell culture derived Smallpox Live Vaccine have been made and certified.

- The Phase 3, double-blind field trial of the Argentine Hemorrhagic Fever Live Vaccine has been extended to allow for inclusion of a total of approximately 6000 at-risk Argentine volunteers. Thus far, no vaccine related reactions have been noted, and all vaccinees have seroconverted.

- An agreement was reached with the Food and Drug Administration (FDA) to test three consecutive lots of the Japanese Encephalitis Vaccine in humans to facilitate licensure.

- Phase 1 studies indicated that a recombinant Falciparum Malaria Sporozoite protein covalently bound to Pseudomonas Toxin A generated a fourfold greater immune response than when admixed with alum. An IND for the recombinant protein coupled to Hepatitis B surface antigen has been submitted.

- Preclinical testing of the candidate Q Fever Irradiated Vaccine was completed; the IND submission has been prepared and is in the final stages of in-house review.

- Review of clinical records of a Phase 1 clinical trial for Tularemia Live Vaccine at USAMRIID, which was suspended in the face of transient, minor liver enzyme changes in two of nine volunteers, has indicated that the apparent changes may not have been vaccine related. A new protocol has been submitted to the Human Subjects Research Review Board for approval to continue safety testing.

- Type F Botulinal Toxin has been purified and initial toxoiding studies are in progress. Media selection and purification techniques for Type G Botulinal Toxin are in progress.

- Two candidate Shigella Vaccines are currently undergoing refinement and a third candidate vaccine, composed of a strain of Shigella flexneri genetically engineered to be avirulent, is ready for tests in volunteers.

- The Investigational New Drug (IND) application for the Schistosome Topical Antipenetrant was filed with the FDA on 1 June 1989. The Phase 1 protocol has been approved by The Surgeon General's Human Subjects Research Review Board.

- Agreement was reached to field multiple methods of permethrin impregnation of the Insect/Arthropod Repellent, Clothing Impregnant with an Individual Dynamic Adsorption Kit (for individual use), 2-gallon sprayer method (for company size unit use), and pad roll method (for industrial application). Continued technical testing showed negligible permethrin residue

in adsorption kit bags, and that perspiration and steam pressing of Battle Dress Uniforms (BDUs) had no degrading effect on the permethrin. The registration application to the EPA has been completed.

- Technical tests concerning the compatibility of a commercially available Body Louse Toxicant (malathion) with powered delousing equipment permitted resolution of a caking problem. An effective anti-caking agent (silicon dioxide) was identified, which, when added to the deodorized malathion dust, will permit the introduction of an "off-the-shelf" product to meet the Army's requirement.

PROJECTIONS

- A new lot of Eastern Equine Encephalitis Vaccine will be produced at the Salk Vaccine Production Facility because of exhaustion of the previous stockpile. A pilot lot of a new cell culture derived Smallpox Vaccine will be produced to replace the present commercial product (grown on calves and containing contaminating bacteria) to allow parenteral rather than percutaneous administration. Clinical testing of the repackaged inactivated Rift Valley Fever Vaccine will be initiated, and clinical testing of the first Liposome Vaccine (Liposomal-Sporozoite Vaccine) should be completed.

- Future studies at the University of Maryland Vaccine Testing Facility include safety and efficacy of a modified E. coli-Shigella flexneri Vaccine, a follow-up study of the volunteers from the Klebsiella-Pseudomonas Vaccine study to determine longevity of immunity, and initial testing of a HbS R32 recombinant malaria vaccine. Final results from the Hepatitis B Vaccine study will be available, comparing intradermal immunization with the subcutaneous route. New candidate Shigella Vaccines will be tested as they become available after appropriate animal model testing.

- The Oxygen Carrying Blood Expander in-house program will be returned to a tech base effort. A technology watch will be maintained covering the development of blood substitutes by the commercial sector.

- The 1000 test kits for each of four biological agents will be procured and manufactured in 1990 and be available to start testing the Rapid Identification System in 4Q90.

- Expanded clinical trials will be carried out with the J-5 Human Monoclonal Antibody. Results of the trials from both the civilian and military sector should enable licensure of the product by Centocor.

- Klebsiella/Pseudomonas Human Immune Globulin will be obtained from immunized volunteers.

- The IND for Lassa Fever Immune Globulin will be submitted and the Phase 1 trial conducted at USAMRIID.

- WRAIR's Hepatitis A Vaccine will be safety tested.

- The Phase 1 evaluation of safety and immunogenicity of Adenovirus Vectored Hepatitis B Vaccine will be completed.

- A new study of Dengue Type 4 Live Vaccine will evaluate immunogenicity in yellow fever immune individuals and expand the number of flavivirus naive vaccinees. Transmission by vector mosquitoes will also be evaluated in this study. An IND for Dengue 4 Vaccine made in Thailand will be submitted, and the vaccine will be safety tested in the U.S.

- A new Rift Valley Fever Live Vaccine requiring only one injection will transition into development, and an IND will be submitted.

- Vaccinia Vectored Venezuelan Equine Encephalitis Vaccine (VEE) genes will be transferred into certified vaccinia virus and a pilot lot of vaccine will be produced at Salk Institute, Government Services Division.

- A master seed of Vaccinia-Vectored Korean Hemorrhagic Fever (KHF) Vaccine will be produced at the Salk Institute.

- A pilot lot of Smallpox Live Vaccine will be made and purified according to USAMRIID's protocol.

- The Phase 3 field trial of Argentine Hemorrhagic Fever Live Vaccine will continue in 1990, with vaccine being administered to an additional 1000 Argentine volunteers from the at-risk population. Clinical and serological data will be obtained for the first group of 5000 vaccinees by 1990.

- Testing for immunizing consistency of three lots of Japanese Encephalitis Vaccine will be performed in military personnel in Hawaii.

- A study of Chikungunya Vaccine will be conducted at Fort Bragg, NC, to gain additional immunogenicity data.

- Dengue 1 Vaccine will be transitioned to advanced development.

- Phase 1 studies of a new liposome encapsulated Falciparum Malaria Sporozoite Vaccine will be completed.

- Extended safety and immunogenicity studies of Vivax Malaria Sporozoite Vaccine will be carried out with additional volunteers.

- An IND application for Q Fever Irradiated Vaccine will be submitted, and Phase 1 clinical trials will begin.

- The Phase 1 clinical trial for Tularemia Live Vaccine will resume in 1QCY90 as a result of the favorable review of the clinical records of the initial Phase 1 vaccinee.

- Types F and B Botulinal Toxoids will be prepared and tested in animals. Technical data package will be finalized for production and purification of these toxoids. INDs for each toxoid will be prepared.

- The genetically engineered Shigella flexneri Vaccine will be tested in Phase 1 clinical trials.

- A new candidate N. meningitidis (Group B) Vaccine will go through Phase 1 testing at USAMRIID.

- The Phase 1 study of the Schistosome Topical Antipenetrant will be conducted at Johns Hopkins University.

- Application for registration of Permethrin to be used as a Clothing Impregnant for Battle Dress Uniforms will be submitted to the EPA.

- A Milestone II IPR will be convened during 1QCY90 to transition the Body Louse Toxicant as a Nondevelopmental Item to the Defense General Supply Center for procurement.

THIS PAGE INTENTIONALLY LEFT BLANK

PHARMACEUTICAL SYSTEMS
PROJECT MANAGEMENT DIVISION
THE PROGRAM

INTRODUCTION

The Pharmaceutical Systems Project Management Division centrally manages the development and the initial production of pharmaceutical products (antidotes and drugs), related drug delivery systems (autoinjectors and transdermal patches), and decontamination products. These products are fielded as preventive, protective, and therapeutic modalities for use against chemical and biological warfare threats, certain endemic diseases, and the treatment of combat casualties.

MILITARY RELEVANCE

U.S. military forces must be prepared to serve anywhere in the world against any threat. This could result not only in conventional injuries sustained during combat but exposure to chemical and biological warfare agents as well as exposure to endemic diseases not commonly found in the United States. The development of products against these threats will help save lives, sustain the fighting force, and enhance return to duty.

OBJECTIVES

The objectives of this division are to develop pharmaceuticals to be used for prophylaxis, immediate treatment, and definitive treatment against a wide variety of naturally occurring diseases, threat force use of chemical and biological agents, and combat-generated injuries. These pharmaceuticals include those for use following exposure to organophosphorus compounds, vesicants, and cyanide, and those to protect or treat soldiers suffering from malaria, schistosomiasis, and leishmaniasis. In addition, a kit to decontaminate the skin following exposure to chemical warfare agents or toxins is undergoing development as is an antidote against the oral ingestion of toxins. From a more conventional aspect, blood replacement fluids, and improved antimicrobial skin dressings are under development.

PRODUCT DESCRIPTIONS

- The <u>Regulatory Affairs</u> support contract, with EER Systems Corporation, provides a mechanism to facilitate the timely and efficient execution of the U.S. Army medical materiel development program by preparing and assembling both generic and product specific Food and Drug Administration, and other regulatory agency, related documentation. This includes the preparation and assembly of Investigational New Drug Applications, Investigational Device Exemptions, New Drug

Applications, Biological License Applications, Premarket Approvals, Environmental Protection Agency Registrations, and all related documentation and support.

- The Toxicology support contracts, with the University of Illinois at Chicago and Hazleton Laboratories, provide support for pharmaceutical products which are not included either in an in-house effort or under a contract. This support includes all toxicology efforts from basic in vitro mutagenicity screening through long term (more than one year) chronic studies.

- The Phase I Clinical Pharmacology support contract with Johns Hopkins University, provides the U.S. Army Drug Development Program with those safety, tolerance, and pharmacokinetic studies, in humans, necessary to support the continued development of pharmaceutical products within the Command.

- The Formulation support contract with the University of Iowa, provides formulated pharmaceuticals which are used in advanced toxicology and clinical studies. The contractor has the capability to provide, solid oral or parenteral dosage forms.

- The M291 Skin Decontaminating Kit (SDK) is a resin-based system being developed for Joint Service use. It will replace the current M258A1 Personal Decontamination Kit and the M58A1 Training Aid. The M291 is envisioned as a superior, safe and effective skin decontaminating system for use against multiple percutaneous chemical threat agents.

- A Convulsant Antidote for Nerve Agent (CANA) is required to prevent or ameliorate convulsions in severe nerve agent casualties. Anticonvulsants such as diazepam prevent these convulsions which can result in brain injury. An autoinjector containing only an anticonvulsant will be issued to soldiers and administered in conjunction with the Nerve Agent Antidote Kit, by Buddy-Aid to those individuals incapacitated by nerve agents.

- Halofantrine is a 9-phenanthrenemethanol antimalarial that is being jointly developed by the Walter Reed Army Institute of Research (WRAIR) and Smith, Kline, and French, as an alternative treatment for use in Mefloquine-resistant Plasmodium falciparum malaria. The development of Halofantrine has been divided into treatment and prophylactic indications. The prophylactic indication is in long-term preclinical toxicology.

- Hypertonic Saline Dextran (HSD) is a safe and effective, small-volume product suitable for rapid field administration that can be used to resuscitate and stabilize hypovolemic shock casualties. A Collaborative Research and Development Agreement (CRDA) is on-going with Pharmacia for the development of this product.

- A Multichambered Autoinjector (MA) (single barrel) for the administration of nerve agent antidotes (2 mg atropine, 600 mg 2-PAM Cl) is being evaluated. The MA is a single autoinjector which contains therapeutic drugs in separate chambers and injects both antidotes through a single needle. A clinical study at the Department of Clinical Investigation, Madigan Army Medical Center, suggested that the injection of atropine and 2-PAM Cl into the same injection site adversely affects the absorption of atropine. Similar results were obtained in a sheep study conducted at Battelle Laboratories. Based on this information, some of the vendors have modified their MAs which will need to be tested.

- Morphine Repackaging is required to provide an analgesic that meets the field requirements of extended stability, greater durability and rapidity of use, and is tamper evident. Morphine stocks in the inventory are over 25 years old and are beginning to deteriorate.

- Pyridostigmine Sustained Release is envisioned as a superior pretreatment for use against nerve agent poisoning. When used in combination with atropine and 2-PAM, pyridostigmine is effective against all known nerve agents and is notably effective against soman.

- The Medical Aerosolized Nerve Agent Antidote (MANAA) is an atropine aerosol inhalant used by medical personnel for the supplemental treatment of nerve agent casualties after adequate injectable atropine has been given. The expected role of MANAA is to deliver atropine to the airway of spontaneously breathing and sufficiently lucid nerve agent casualties. The aerosol is intended for use at forward medical care facilities including battalion aid stations.

- WR 238,605, is an 8-aminoquinoline derivative currently in the concept exploration phase of development as an antimalarial. It is being developed as a replacement for primaquine for the treatment of Plasmodium vivax malaria.

- An improved Antimicrobial Dermal Dressing (ADD) will be capable of providing sustained release of antimicrobial agents at the site of dermal injury to prevent infection and enhance wound healing.

- Pentostam, sodium stibogluconate, is a drug produced and marketed worldwide by Burroughs-Wellcome Foundation of Great Britain. Pentostam is being studied under an IND application for the treatment of visceral and cutaneous leishmaniasis.

- Qinghaosu analog is a sesquiterpene lactone produced by the extraction and purification of the substance artemisian from the botanical artemisia annua. This rapid acting blood schizonticide is being developed for the treatment of cerebral malaria.

- WR 6026 is an 8-aminoquinoline being tested as an oral treatment for visceral leishmaniasis.

- Mefloquine, a quinoline methanol, is an antimalarial drug indicated for use in multi-drug resistant Plasmodium falciparum malaria.

- Toxin Antidote (Highly Activated Charcoal) is a commercially available activated charcoal preparation with three times the surface area of Activated Charcoal USP. This product is being proposed as a broad spectrum antidote for the physical binding of chemicals and toxins.

- Liposomal Pentostam is a formulation of Pentostam encapsulated in liposomes for the directed treatment of visceral leishmaniasis. The Burroughs-Wellcome Foundation and WRAIR, through a Cooperative Research and Development Agreement, are conducting preclinical studies.

MAJOR ACCOMPLISHMENTS

- During this past calendar year, the Regulatory Affairs contractor prepared an IND for the Schistosomal Topical Antipenetrant, a draft EPA Registration package for permethrin as a clothing impregnant, a draft non-clinical section of an NDA for hypertonic saline dextran, and 18 other reports. They also provided a review of the enpiroline clinical data collected to date which served as the basis for the Government's decision to terminate this program. The contractor also entered all of the clinical information from a ribavirin efficacy study against Lassa Fever into a data base; this would allow this data to be properly analyzed and formatted for inclusion into the safety section of an NDA. A new contract was competitively awarded to EER to prepare regulatory documents for not only pharmaceuticals, but biologicals and devices as well.

- The following Toxicology studies were completed: Subchronic Toxicity Study of WR 46234 (Schistosome Topical Antipenetrant Lotion) in two species; Subchronic Toxicity Study of Halofantrine Hydrochloride; Photoallergic Contact Dermatitis Study (WR 46234); Fertility and General Reproductive Performance Study of Pyridostigmine Bromide; Developmental Toxicity Study of Pyridostigmine Bromide; Perinatal and Postnatal Study of

Pyridostigmine Bromide; Developmental Toxicity Study of Pyridostigmine; and Oral Toxicity Study of WR 238605. Thirteen draft reports were submitted.

- Under the Phase I Clinical Pharmacology contract, one study was completed evaluating "The Safety, Tolerance, Pharmacokinetics and Pharmacodynamics of Single Oral Doses of Pyridostigmine Administered by an Osmotic Delivery Module (Osmet^{r}) Compared to Pyridostigmine Syrup in Healthy Men." A final report was delivered on the "Bioavailability of Oral Pyridostigmine and Inhibition of Red Blood Cell Acetylcholinesterase by Oral and Intravenous Pyridostigmine." A protocol was prepared to "Assess the Irritancy, Contact Sensitization and Contact Photoallergic Potential of Niclosamide-A Topical Anti-Schistosomal Agent." An RFP was prepared and proposals were submitted for continuation of this effort. Discussions are ongoing between those still in the competitive range and the Acquisition Activity.

- In the Formulation contract, studies were completed for the formulation development of the 90 mg sustained release pyridostigmine and it was manufactured under Good Laboratory Practices for a clinical study. Five and 15 mg tablets of WR 6026 were manufactured for the Phase II clinical study in Kenya. A Quinghaosu analog, arteether, was formulated in sesame oil for toxicology studies.

- A section 510(k) notification of the Army's intent to manufacture and field the M291 Skin Decontaminating Kit (SDK) as a medical device for Department of Defense use was filed with the FDA and, subsequently, permission to market the device was received. Low rate initial production and first article test of the M291, manufactured on two state-of-the-art Government procured production lines, was completed 4Q89. A Milestone III In-Process Review (IPR) was conducted 28 November 1989 with a unanimous decision to adopt the M291 SDK for production and deployment. The technical data package for competitive follow-on production and fielding of the M291 was transitioned to the U.S. Army Armament, Munitions and Chemical Command.

- A Milestone I/II IPR was conducted on 18 January 1989 with the decision to transition the Convulsant Antidote for Nerve Agents (CANA) into Full Scale Development (FSD). An FSD contract was awarded on 1 June. CANAs were produced for an Initial Operational Test and Evaluation (IOT&E) which was conducted at Fort Polk, LA, in November. The FDA agreed that an NDA for the CANA was an acceptable regulatory approach.

- All preclinical and clinical studies required for the NDA for Halofantrine, as a treatment for Plasmodium falciparum malaria, were completed. Smith, Kline, and French is preparing an NDA for filing with the FDA.

• All non-clinical studies on **Hypertonic Saline Dextran**, intended for inclusion in the New Drug Application (NDA) were completed by Letterman Army Institute of Research. The draft NDA was prepared, in conjunction with Pharmacia, and review was initiated in December for an early 1990 submission to the FDA.

• The Joint Service Operational Requirement for the **Multichambered Autoinjector (MA)** was approved by HQDA.

• An Acquisition Decision Memorandum for the 10 mg Morphine Autoinjector was approved by the Commanding General, USAMRDC, and the product was transitioned to the U.S. Army Medical Materiel Agency on 12 May 1989. Essential characteristics were established and published by the Defense Medical Standardization Board on 9 August 1989. Two of three manufacturers involved in CRDAs have submitted paper NDAs to the FDA.

• Formulations of **Sustained Release Pyridostigmine**, obtained under contract or No-Dollar Agreement, underwent clinical studies. No formulation tested provided 20-40% cholinesterase inhibition for 12 hours. Documentation for the Investigational New Drug (IND) file at the FDA was updated, and the in-life portion of toxicological studies were completed to establish the safety of pyridostigmine with reference to its teratological and reproductive effects. Studies were begun and are currently ongoing on the possible interaction of Pyridostigmine on human thermoregulatory physiology under various conditions.

• A Clinical study was conducted on the **Medical Aerosolized Nerve Agent Antidote (MANAA)** which demonstrated that medical personnel can effectively administer this product to persons who have never received an oral inhalant previously. Preparation of the NDA was begun. Approval for MANAA airlift transportation was obtained.

• Additional preclinical toxicology studies of WR 238,605 were completed.

• Three CRDAs were established to evaluate Antimicrobial Dermal Dressing products that could satisfy the military requirements for a sustained release product. The Required Operational Capability (ROC) was approved by HQDA. Preclinical testing of antimicrobial agents is underway at the U.S. Army Institute of Dental Research. A customer test of the adhesive properties of candidate dressings was completed at Fort Bragg by the Airborne and Special Operations Test Board.

• A protocol was approved to allow **Pentostam** to be used for the treatment of U.S. Service Personnel. Studies are continuing in Panama and Guatemala to evaluate Pentostam against cutaneous leishmaniasis.

- A protocol was drafted to evaluate the efficacy of WR 6026 in Kenya against visceral leishmaniasis.

- The NDA for the antimalarial drug, **Mefloquine Hydrochloride**, was approved by the FDA on 2 May 1989. The indication contained in the NDA was for the prophylaxis and treatment of chloroquine resistant Plasmodium falciparum malaria.

- Efforts to identify alternative sources for the Toxin Antidote (Highly Activated Charcoal) were initiated. The original manufacturer no longer produces this product.

- Preclinical studies with **Liposomal Pentostam** identified toxicity problems associated with the liposomes.

- A Capstone JSOR for antimalarial drugs was approved on 17 April 1989.

- A Capstone JSOR was approved at HQDA for a **Family of Vesicant Antidotes.**

- A Capstone JSOR for Individual Protection against Schistosomiasis was approved at HQDA.

PROJECTIONS

- Under the **Regulatory Affairs** contract, five to six IND's will be prepared for vaccines and for pharmaceutical products(KHF vaccine, Live-attenuated Rift Valley Fever vaccine, topical skin protectant, WR 238605, microencapsulated antibiotics, among others). One IND will be prepared for monoclonal antibody or immune globulin. Task orders will be initiated for an NDA (pyridostigmine) for and for a BLA (Tularemia vaccine). Two 510(k)'s will be prepared (for the RDIC and the litter).

- Under the **Toxicology** contracts, the following studies will be conducted: a one year Ribavirin-induced testicular degeneration and recovery study; a two week study on HI-6 and MMB-4, new oximes against nerve agent poisoning; and a one year chronic study of halofantrine; An RFP will be drafted and published in the Commerce Business Daily recompeting the ttoxicology contracts which expire in 1991.

- A clinical study will be conducted under the **Phase I Clinical Pharmacology** contract to evaluate the irritancy, contact sensitization and contact photoallergic potential of niclosamide. A study will be conducted to evaluate the 90 mg sustained release pyridostigmine formulation prepared by the University of Iowa. Another study will be conducted to determine the pharmacokinetics of several multichambered autoinjectors (supplied by commercial firms under CRDA's) containing atropine and 2-PAM. A new

contract will be awarded to replace the current expiring contract.

- The Formulation contractor will formulate WR 238605 in five and 15 mg tablets for phase I clinical studies. Additional formulation efforts will be undertaken on the Quinghaosu analog (arteether, in sesame oil) to include stability studies. Preformulation studies (chemical characterization) on ribavirin and AVS 206 will be initiated. An RFP will be released to recompete the formulation contract.

- A contract option (fixed price) will be awarded for the production and deployment of the first 1.5 million M291 Skin Decontaminating Kits (SDK). Deployment will be completed 3Q90.

- A competitive contract for follow-on procurement of the SDK will be awarded by USAMCCOM.

- A clinical study to address FDA issues for the Convulsant Antidote for Nerve Agent will be conducted 2-3Q90. A Milestone III IPR will be held during 3Q90.

- A Milestone I/III IPR for the antimalarial Halofantrine for the treatment indication will be held 1Q90. An NDA will be filed in the United States by Smith, Kline, and French (SKF).

- A New Drug Application for Hypertonic Saline Dextran (HSD) will be submitted 1Q90. A Milestone I/II IPR is scheduled for 1Q90.

- A Milestone Ib IPR will be held for the Multichambered Autoinjector 3Q90.

- Approval of NDAs for a Morphine Autoinjector is anticipated during FY90. Resolution of packaging and shelf-life issues will occur through coordination with the U.S. Army Medical Materiel Agency and the FDA.

- A Milestone II/III IPR will be held for Pyridostigmine 3Q90.

- An NDA for the Medical Aerosolized Nerve Agent Antidote is scheduled to be filed with the Food and Drug Administration in January 1990. A Milestone II/III IPR will be held 1Q90.

- A Milestone I IPR for the antimalarial drug WR 238,605 will be held.

- Results of preclinical testing of **Antimicrobial Dermal Dressing** candidates will provide data for selection of an optimal antimicrobial agent which includes antifungal activity. Evaluation of adhesive properties will produce information important in determining overall effectiveness of the dressing system.

- A Special IPR for the antileishmanial drug **Pentostam** will be held 1Q90.

- **Quinghaosu** will be returned to the tech base for additional studies to identify the most suitable analog for progression into advanced development.

- A Phase II clinical study will be initiated in Kenya for the antileishmanial drug **WR 6026**.

- The **Toxin Antidote (Highly Activated Charcoal)** program will be terminated due to a lack of manufacturing sources.

- **Liposomal Pentostam** will be returned to the tech base to reformulate the liposome delivery system.

- A Milestone II/III IPR for the antimalarial drug **Enpiroline** will be held 1Q90.

- A Topical Skin Protectant will transition to advanced development.

THIS PAGE INTENTIONALLY LEFT BLANK

PUBLICATIONS

Calisher, C.H., Karabatsos, N., Dalrymple, J.M., Shope, R.E., Porterfield, J.S., Westaway, E.G., and Brandt, W.E. 1989. Antigenic relationships between flaviviruses as determined by cross-neutralization tests with polyclonal antisera. J. Gen. Virol. 70:37-43.

Kliks, S.C., Nisalak, A., Brandt, W.E., Wahl, L., and Burke, D.S. 1989. Antibody-dependent enhancement of dengue virus growth in human monocytes as a risk factor for dengue hemorrhagic fever. Am. J. Trop. Med. Hyg. 40:444-451.

Friedl, K.E., Hannan, Jr., C.J., Schadler, P.W., and Jacob, W.H. 1989. Atropine absorption after intramuscular administration with 2-pralidoxime chloride by two automatic injector devices. J. Pharm. Sci. 78:728-731.

O'Brien, J., Thompson, W.L., and Pace, J.G. 1989. In Vitro Metabolism of T-2 Mycotoxin. In Vitro Toxicology 2:139-150.

Perry, B.D., Schmidtmann, E.T., Mansen, J.W., and Rice, R.M., Fletcher, M., Turner, E.C., Robl, M.G., and Hahn, N.E. 1989. Epidemiology of Potomac Horse Fever: An investigation into the possible role of non-equine mammals. Veterinary Record 125:83-86.

Oaks, E.V., Kelly, D.J., Rice, R.M., and Stover, K. 1989. Antigenic and Genic Relatedness of Eight Rickettsia tsutsugamushi antigens. Infection and Immunity 57:3116-3122.

Carroll, J.F., Schmidtmann, E.T., and Rice, R.M. 1989. White-Footed Mice-Tick Burdens and Role in Epizootiology of Potomac Horse Fever in Maryland. Journal of Wildlife Diseases 25:397-400.

Hahn, N.E., Perry, B.D., Rice, R.M., Hansen, J.M., and Turner, E.C. 1989. A study of the role of blackflies in the epidemiology of Potomac Horse Fever. Veterinary Record 125: 273-274.

THIS PAGE INTENTIONALLY LEFT BLANK

PRESENTATIONS

Brandt, Walter E. Briefing on Program Prioritization to World Health Organization consultants, Fort Detrick, Frederick, MD, September 1989

Caldwell, Donald W. Briefing on the Resuscitative Fluids Production System, Joint Services Medical Logistics Coordinating Group Meeting, Fort Detrick, Frederick, MD, January 1989

Channing, Eugene S., COL "Ballistic-Laser Protective Spectacles (B-LPS) with Optional Prescription Lens Carrier (PLC)," Occupational Vision Consultants Course, U.S. Army Environmental Hygiene Agency, Brookshire Hotel, Baltimore, MD, September 1989

Clawson, Ronald E. Briefing on Development of an Industrial Familiarization Program to the Pharmaceutical Manufacturing Association, Washington, DC, January 1989

Goeringer, Fred, LTC Presentation and Demonstration on Filmless Medical Imaging, Health Services Command Commanders Conference, Seattle, WA, January 1989

Goeringer, Fred, LTC Medical Imaging in Military Medicine, Worldwide Image Management and Communications Conference, Washington, DC, June 1989

Goeringer, Fred, LTC Military Plans for Digital Medicine Imaging, British National Health Authority, London, England, July 1989

Goeringer, Fred, LTC Briefing, Research and Development Status and Plans for Computed Tomography and Technology Transition Plans for Digital Imaging Network Systems (DINS) to Senior Leadership, AMEDD Technical Committee Meeting, Office of The Surgeon General, Washington, DC, November 1989

Harrington, Donald G., LTC Briefing on M291 Skin Decontaminating Kit Development Program to Korean Army Delegation, Fort Detrick, Frederick, MD, November 1989

Lehmann, Craig R., LTC Presentation on atropine for the treatment of organophosphorus poisoning to the Division of Clinical Pharmacology, Uniformed Services University of the Health Sciences, Bethesda, MD, March 1989

Lehmann, Craig R., LTC Information presentation on the status of the CANA project to the U.S. Air Force Surgeon General's Office, Bolling AFB, DC, September 1989

Schiefer, Bernard A., COL Body Louse Toxicant, Triservice Entomology Workshop, Jacksonville, FL, February 1989

Schiefer, Bernard A., COL Operational Entomology, 1989 Aerospace Medical Association Annual Scientific Meeting, Washington, DC, May 1989

Schiefer, Bernard A., LTC Briefing, Research and Development Status and Plans for Field Medical Oxygen Generating and Distribution System, AMEDD Technical Committee, Office of The Surgeon General, Washington, DC, November 1989

Schieferstein, George J. Poster, in absentia, "Carcinogenic Evaluation of 3,3' Dimethylbenzidine Dihydrochloride in BALB/C Mice," The Society of Toxicology Spring Meeting, Altanta, GA, February - March 1989.

SEMINARS AND MAJOR TRAINING EVENTS

Albright, Deanna W. Basic Supervisory Course, Fort Detrick, MD, January 1989

Albright, Deanna W. Manpower and Force Management, ALMC, Fort Lee, VA May 1989

Albright, Deanna W. Personnel Administration, FCC, Frederick, MD, January-May 1989

Albright, Deanna W. Files Improvement, Washington, DC, June 1989

Albright, Deanna W. Records Disposition, Washington, DC June 1989

Albright, Deanna W. Principles of Management, FCC, Frederick, MD, August-December 1989

Baker, Rosalinda How to Get Things Done, Hagerstown, MD January 1989

Boswell, Lydia L. The Secretarial Seminar, Frederick, MD, November 1989

Brandt, Walter E. National Vaccine Advisory Committee, Interagency Working Group, monthly, 1989.

Brandt, Walter E. Chairman, World Health Organization (WHO) Steering Committee on Dengue, Vienna, Austria, June 1989.

Brandt, Walter E. WHO Scientific Advisory Group of Experts, Geneva, Switzerland, July 1989.

Brandt, Walter E. American Society of Tropical Medicine and Hygiene, Washington, DC, Scientific Program Committee, August 1989.

Caldwell, Donald W. Basic Supervisory Course, Fort Detrick, MD, January 1989

Caldwell, Donald W. Memory Development and Effective Listening, Fort Detrick, MD, March 1989

Caldwell, Donald W. Personnel Management for Executives Program, Tamiment, PA, April 1989

Caldwell, Donald W. FDA Medical Device Update Seminar, Washington, DC, June 1989

Caldwell, Donald W. Army Streamlined Acquisition Program, Reston, VA, October 1989

Caldwell, Donald W. US/Israeli Defence Force Shoresh Conference, Shoresh, Israel, November 1989

Chaffee, John L., LTC dBase III Plus, Fort Detrick, Frederick, MD, February 1989

Chaffee, John L., LTC Advanced dBase III Plus, Fort Detrick, Frederick, MD, June 1989

Channing, Eugene S., COL General and Ocular Pharmacology Course, State University of New York College of Optometry, New York City, NY, April-May 1989

Channing, Eugene S., COL Occupational Vision Consultants Course, U.S. Army Environmental Hygiene Agency, Brookshire Hotel, Baltimore, MD, September 1989

Clawson, Ronald E. Annual Scientific Review, U.S. Army Medical Research Institute of Chemical Defense, January 1989

Clawson, Ronald E. Fourth International Symposium on Recent Advances in Drug Delivery Systems, Salt Lake City, UT, February 1989

Clawson, Ronald E. Monitoring of Clinical Drug Studies, Center for Professional Advancement, East Brunswick, NJ, May-June 1989

Clawson, Ronald E. 1989 Medical Defense Bioscience Review, Columbia, MD, August 1989

Clawson, Ronald E. Boomerang (EER Law for Supervisors), Fort Detrick, Frederick, MD, October 1989

Cole, Francis E., Jr. Symposium on Agents of Biological Origin, Baltimore, MD, March 1989

Cole, Francis E., Jr. American Society for Microbiology Conference on Biotechnology, Orlando, FL, June 1989.

Cole, Janice M. Lotus 1-2-3 MS/DOS-Intro, Fort Detrick, MD, March 1989

Cole, Janice M. Contract Finance for Program Managers Course, DSMC, Fort Belvoir, VA, August-September 1989

Cutsail, Cindy E. Proofreading and Grammar, Fort Detrick, Fredeick, MD, May 1989

Delaplaine, Edward S. dBase III Plus, Fort Detrick, Frederick, MD, April 1989

Delaplaine, Edward S. Advanced dBase III Plus, Fort Detrick, Frederick, MD, June 1989

Delaplaine, Edward S. Program Management, The American Graduate University, Alexandria, VA, October 1989

Doughty, David S. Fundamentals of Systems Acquisition Management Course, DSMC, St. Louis, MO, May 1989

Doughty, David S. Contract Management for Program Managers Course, DSMC, Boston, MA, August 1989

Doughty, David S. Program Management, The American Graduate University, Alexandria, VA, October 1989

Doughty, David S. Contractor Performance Measurement Course, DSMC, Fort Belvoir, VA, December 1989

Eggert, Anna M. Budget Execution, Fort Detrick, Frederick, MD, July 1989

Eggert, Anna M. Systems Acquisition Funds Management, DSMC, Fort Belvoir, VA, December 1989

Ferguson, Warren F. Army Streamlined Acquisition Program, Reston, VA, October 1989

Ferguson, Warren F. Prevention of Sexual Harrassment for Supervisors, Fort Detrick, Frederick, MD, October 1989

Fung, Kathleen P. dBase III Plus, Fort Detrick, MD, April 1989

Fung, Kathleen P. English Composition, FCC, Frederick, MD January-May 1989

Goeringer, Fred, LTC Medical Imaging III, Society of Photo-Optical Instrumentation Engineers, Los Angeles, CA, January 1989

Guessford, Kay E. Image and Communication Skills for Women, Hagerstown, MD, January 1989

Guessford, Kay E. dBase III Plus, Fort Detrick, MD, March 1989

Guessford, Kay E. Effective Management Skills for Administrative Assistants and Secretaries, Fort Detrick, MD, August 1989

Harrington, Donald G., LTC Technical Data Package Fundamentals Course, Chemical Research, Development and Engineering Center, Aberdeen Proving Ground, MD, March 1989

Harrington, Donald G., LTC American Association for Laboratory Animal Sciences Annual Meeting, Little Rock, AR, November-December 1989

Johnson-Winegar, Anna. Botulism Antibody Study, Oakland, CA, January 1989.

Johnson-Winegar, Anna. Stroma Free Hemoglobin Review, Sar Francisco, CA, January 1989.

Johnson-Winegar, Anna. Advanced Biologics Regulations and Law Workshop, Washington, DC, March 1989.

Johnson-Winegar, Anna. International Workshop on Anthrax, Winchester, England, April 1989.

Johnson-Winegar, Anna. American Society for Microbiology, New Orleans, LA, May 1989.

Johnson-Winegar, Anna. International Symposium on Red Cell Substitutes, San Francisco, CA, May 1989.

Johnson-Winegar, Anna. Second Annual Joint Israeli Defence Forces-U.S. Army Conference on Vaccines of Military Importance, Tel Aviv, Israel, May 1989.

Johnson-Winegar, Anna. Office of Personnel Management Executive Seminar, Lancaster, PA, August 1989.

Johnson-Winegar, Anna. Army Streamlined Acquisition Program, Reston, VA, October 1989.

Johnson-Winegar, Anna. Prevention of Sexual Harassment for Supervisors, Fort Detrick, Frederick, MD, October 1989.

Lehmann, Craig R., LTC Regulatory Affairs Management in the Pharmaceutical Industry, Center for Professional Advancement, East Brunswick, NJ, September 1989

Moore, Charles A., LTC Postgraduate Course in Clinical Pharmacology, Drug Development, and Regulation, Tufts University Center for the Study of Drug Development, Boston, MA, February-March 1989

Moore, Charles A., LTC Introduction to the Regulatory Process, University of Wisconsin, Madison, WI, June 1989

Moore, Charles A., LTC Research and Development Orientation Course, ALMC, Fort Lee, VA, August 1989

Moore, Charles A., LTC Documentation and Good Laboratory Practices, CPA, Fort Detrick, MD, October 1989

Morgan, Sharon L. Speedwriting Shorthand, FCC, Frederick, MD January-April 1989

O'Brien, John C., LTC Joint Meeting of the American Society for Cell Biology, and the American Society for Biochemistry and Molecular Biology, San Francisco, CA, February 1989

O'Brien, John C., LTC Basic Drug Law, Washington, DC, February 1989

O'Brien, John C., LTC Practical Considerations in Preparing Investigational New Drug and New Drug Applications, March 1989

O'Brien, John C., LTC Preparing Clinical Protocols and Managing Clinical Investigations, East Brunswick, NJ, March 1989

O'Brien, John C., LTC dBase III Plus, Fort Detrick, Frederick, MD, April 1989

O'Brien, John C., LTC Conference on Emerging Viruses: Evolution of Viruses and Viral Disease, Washington, DC, May 1989.

O'Brien, John C., LTC Fundamentals of Systems Acquisition Management Course, DSMC, Fort Belvoir, VA, September 1989.

O'Brien, John C., LTC Manprint Familiarization Seminar, Fort Belvoir, VA, August 1989.

O'Brien, John C., LTC 38th Annual Meeting of the American Society of Tropical Medicine, Honolulu, HI, December 1989.

Pedersen, Carl E., Jr., COL The Macintosh Seminar, Hunt Valley, MD, December 1989

Pick, Robert O., COL Postgraduate Course in Clinical Pharmacology, Drug Development, and Regulation, Tufts University Center for the Study of Drug Development, Boston, MA, February-March 1989

Pick, Robert O., COL Introduction to the Regulatory Process, University of Wisconsin, Madison, WI, June 1989

Priebe, Rebecca A. Installation and Administration of 3Com Network, Rockville, MD, January 1989

Priebe, Rebecca A. 3Com Plus Communication, Rockville, MD, January 1989

Priebe, Rebecca A. How to Recover Damaged Data Files and Disks, Baltimore, MD, September 1989

Montgomery, James D., MAJ dBase III Plus, Fort Detrick, Frederick, April 1989

Rice, Robert M., LTC dBase III Plus, Fort Detrick, Frederick, MD, February 1989.

Rice, Robert M., LTC Fundamentals of Systems Acquisition Management Course, DSMC, Fort Belvoir, VA, March 1989.

Rice, Robert M., LTC Contract Management for Program Managers Course, DSMC, Fort Belvoir, VA, March 1989.

Rice, Robert M., LTC Good Clinical Practices, Chicago, IL, September 1989.

Rice, Robert M., LTC Practical Considerations in Preparing Investigational New Drug and New Drug Applications, East Brunswick, NJ, October 1989.

Routzahn, Ricky dBase III Plus, Fort Detrick, Frederick, MD March 1989

Routzahn, Ricky Budget Estimating Techniques, Fort Detrick, Frederick, MD, April 1989

Routzahn, Ricky Advanced Lotus 1-2-3, Fort Detrick, Frederick, MD, June 1989

Routzahn, Ricky Budget Execution, Fort Detrick, Frederick, MD July 1989

Roy, Michael J. dBase III Plus, Fort Detrick, Frederick, MD, February 1989

Roy, Michael J. Regulatory Compliance, Princeton, NJ, April 1989

Roy, Michael J. Project Management in Pharmaceutical Industry, East Brunswick, NJ, May 1989

Roy, Michael J. Accelerated Reading, Fort Detrick, Frederick, MD, June 1989

Salter, Cecil S., LTC Research and Development Orientation Course, ALMC, Fort Lee, VA, August 1989

Salter, Cecil S., LTC Evaluating Contractors Proposals, Fairfax, VA, November 1989

Schiefer, Bernard, A., COL Triservice Medical Entomology Post Graduate Professional Short Course, Jacksonville, FL, February 1989

Schieferstein, George J. Postgraduate Course in Clinical Pharmacology, Drug Development, and Regulation, Tufts University Center for the Study of Drug Development, Boston, MA, February-March 1989

Schieferstein, George J. Introduction to the Ragulatory Process, University of Wisconsin, Madison, WI, June 1989

Schieferstein, George J. Gordon Conference on Mechanisms of Toxicity, Meriden, NH, July 1989

Schieferstein, George J. Research and Development Orientation Course, ALMC, Fort Lee, VA, August 1989

Schieferstein, George J. 1989 Medical Defense Bioscience Review, Columbia, MD, August 1989

Schieferstein, George J. Evaluating Contractors Proposals, Fairfax, VA, November 1989

Sheffer, Linda J. Budget Estimating Techniques, Fort Detrick, MD, April 1989

Sheffer, Linda J. Principles of Economics, FCC, Frederick, MD, January-May 1989

Sheffer, Linda J. Budget Execution, Fort Detrick, Frederick, MD, July 1989

Sheffer, Linda J. English Composition, FCC, Frederick, MD, August-December 1989

Splitstoser, Jeffrey C., CPT Memory Development & Effective Listening, Fort Detrick, Frederick, MD, March 1989

Splitstoser, Jeffrey C., CPT Advanced dBase III Plus, Fort Detrick, Frederick, MD, June 1989

Splitstoser, Jeffrey C., CPT Program Management, The American Graduate University, Alexandria, VA, October 1989.

Splitstoser, Jeffrey C., CPT Contract Management for Program Managers Course, DSMC, Fort Belvoir, VA, December 1989

Stickel, Linda K. The Secretarial Seminar, Frederick, MD, November 1989

Twist, Anne P. Effective Briefing Techniques, Fort Detrick, Frederick, MD, August 1989

Twist, Anne P. International Symposium on Military Operations Research, Shrivenham, England, September 1989

Twist, Anne P. Army Streamlined Acquisition Program, Reston, VA, November 1989

Vreuls, Jean P., MAJ Part II, Program Management Course, DSMC, Fort Belvoir, VA, May 1989

Williams, Linda M., CPT Lotus 1-2-3 MS/DOS-Intro, Fort Detrick, MD, February 1989

Zajac, Andrew J., CPT Management Project, University of Maryland, College Park, MD, January-May 1989

Zajac, Andrew J., CPT Production Management and Automation, University of Maryland, College Park, MD, January-May 1989

DISTINGUISHED VISITORS

Representatives from Duphar, The Netherlands. Discussions on the status of their efforts on the morphine autoinjector, multi-chambered autoinjector, and sustained release pyridostigmine, 17 January 1989.

Major Dani Cohen, Israeli Defense Forces, Israel. Discussion of Shigella studies in progress, 10 February 1989.

Representatives from Duphar, The Netherlands. Discussions on the status of their efforts on the morphine autoinjector, multi-chambered autoinjector, and sustained release pyridostigmine, 29-30 March 1989.

Mr. Ab Polak, Duphar, The Netherlands. Discussions on the conduct of a clinical study for the nerve agent anticonvulsant, 27 April 1989.

Dr. Benjamin Bramer and Dr. Jansen van Galen, Duphar, The Netherlands. Discussion on CANA development, 8 June 1989.

Lieutenant Colonel W.D. Crossman, Chief Pharmacist, Department of Defense, Australia. To discuss the development status of products in support of defense against chemical agents. His purpose was to obtain background information as the new chairman of the Nuclear, Biological and Chemical Quadripartrite Working Group, 12 June 1989.

Lieutenant Colonel Manfred Green, Israeli Defence Forces, Israeli. Joint Israeli Defence Forces-U.S. Army Testing, and discussion of Hepatitis protocol and progress on grant, 28 June 1989.

Dr. Benjamin Bramer, Duphar, The Netherlands. Delivery of Investigational New Drug Application (IND) for the nerve agent anticonvulsant to the Government, 3 July 1989.

Major Yona Zaide, Israeli Defence Forces, Israel. Discussion of arbovirus serological studies to be undertaken during her 6-week stay at USAMRIID, 26 September 1989.

Mr. Hans Werner, Dr. Benjamin Bramer, Dr. Jansen van Galen, and Mr. Ab Polak, Duphar, The Netherlands. Discussions on the nerve agent anticonvulsant, the morphine autoinjector, and the multichambered autoinjector, 12 October 1989.

Dr. Julio Maiztegui, Instituto Nacional de Estudios Virosis Hemorrhagicas, Pergamino, Argentina. Field Testing of Argentine Hemorrhagic Fever Vaccine, 12 October 1989.

Major Geoffrey Ritson, Medimec, Ltd., United Kingdom. Discussion on progress of morphine autoinjector, 16 October 1989.

Dr. Jansen van Galen, Duphar, The Netherlands. Discussions on the nerve agent anticonvulsant projects interactions with the Food and Drug Administration, and the multichambered autoinjector, 30-31 October 1989.

Dr. Yun-Su Chung and Dr. Ki Woon Hwang, Agency for Defense Development, Republic of Korea. Discussions of applications of reactive and sorptive polymeric resins to skin decontamination, 6 November 1989.

Dr. Benjamin Bramer, Duphar, The Netherlands. Delivery of IND amendment for the nerve agent anticonvulsant, 11 December 1989.

DISTRIBUTION LIST

Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-ZB
Fort Detrick
Frederick, MD 21701-5012

Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-RMI-S
Fort Detrick
Frederick, MD 21701-5012

Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLA
Fort Detrick
Frederick, MD 21701-5012

Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLB
Fort Detrick
Frederick, MD 21701-5012

Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLC
Fort Detrick
Frederick, MD 21701-5012

Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLE
Fort Detrick
Frederick, MD 21701-5012

Commander
U.S. Army Medical Research Institute of Infectious Diseases
Bldg 1425
Fort Detrick
Frederick, MD 21701-5011

Commander
Letterman Army Institute of Research
Bldg 1110
Presidio of San Francisco, CA 94129-6800

Commander
U.S. Army Medical Research Institute of Chemical Defense
Bldg E3100, Edgewood Area
Aberdeen Proving Ground, MD 21010-5425

Commander
U.S. Army Institute of Dental Research
Bldg 40
Washington, DC 20307-5300

Commander
U.S. Army Aeromedical Research Laboratory
Bldg 8708
Fort Rucker, AL 36362-5292

Commander
U.S. Army Institute of Surgical Research
Bldg 2653
Fort Sam Houston, TX 78234-6200

Commander
U.S. Army Medical Research Acquisition Activity
Bldg 820
Fort Detrick
Frederick, MD 21701-5014

Commander
U.S. Army Biomedical Research and Development Laboratory
Bldg 568
Fort Detrick
Frederick, MD 21701-5010

Commander
U.S. Army Research Institute
of Environmental Medicine
Bldg 42
Natick, MA 01760-5007

Director
Walter Reed Army Institute
of Research
Bldg 40
Washington, DC 20307-5100

HQDA (DASG-HCL-P)
5109 Leesburg Pike
Falls Church, VA 22041-3258

HQDA (DASG-HCD-D)
5109 Leesburg Pike
Falls Church, VA 22041-3256

Commandant
Academy of Health Sciences,
U.S. Army
ATTN: HSHA-CDM
Fort Sam Houston, TX
78234-6100

Commandant
Academy of Health Sciences,
U.S. Army
ATTN: HSHA-TTC
Fort Sam Houston, TX
78234-6100

Commandant
Academy of Health Sciences,
U.S. Army
ATTN: HSHA-UBD
Fort Sam Houston, TX
78234-6100

Commander
U.S. Army Medical Materiel
Agency
ATTN: SGMMA-RM
Fort Detrick
Frederick, MD 21701-5001

Commander
U.S. Army Training and Doctrine
Command
ATTN: ATCD
Fort Monroe, VA 23651

Commander
U.S. Army Forces Command
ATTN: AFLG-FME
Fort McPherson, GA 30330-6000

Commanding General
Marine Corps Research,
Development, and Acquisition
Command
ATTN: Code SSC/GP
Washington, DC 20380-0001

Chief of Staff
U.S. Central Command
MacDill AFB, FL 33608

Chief of Staff
8th United States Army
U.S. Forces Korea
APO San Francisco 96301-0009

Commander
U.S. Army Laboratory Command
ATTN: AMDEL-CD
Adelphi, MD 20783-1145

Commander
10th Mountain Division
ATTN: Division Surgeon
Fort Drum, New York 13602-5000

Commander
1st Special Operations Command
ATTN: AFVS-CG
Fort Bragg, NC 28307

Commander
U.S. Army Human Engineering Laboratory
Aberdeen Proving Ground, MD 21005

Commander
U.S. Army Troop Support Command
ATTN: AMXSO-tL
St. Louis, MO 63120-1787

Commander
U.S. Army Materiel Command
ATTN: AMCDE
5001 Eisenhower Avenue
Alexandria, VA 22333

Commander
U.S. Army Natick Research and Development Command
ATTN: STRNC-Z
Natick, MA 01760

Commander
U.S. Army Research Office
P.O. Box 12211
Research Triangle Park, NC 27709-2211

Commander
U.S. Army Health Services Command
ATTN: HSHA
Fort Sam Houston, TX 78234

Staff Director
Defense Medical Standardization Board
Fort Detrick, Frederick, MD 21701-5013

Commander
6th Infantry Division (Light)
Fort Richardson, AK 99505

Commander
U.S. Army Environmental Hygiene Agency
Aberdeen Proving Ground, MD 21010-5422

Commander
U.S. Army John F. Kennedy Special Warfare Center
ATTN: ATSU-CG
Fort Bragg, NC 28307

Commander
9th Infantry Division
ATTN: AFVO-CG
Fort Lewis, WA 98433-5000

Commander
44th Medical Brigade
Fort Bragg, NC 28307-5000

Commander
18th Medical Command
ATTN: EAMC-CD
APO San Francisco 96301-0080

Commander
7th Medical Command
APO New York 09102

Commanding Officer
Naval Medical Research and Development Command
National Naval Medical Center
Bethesda, MD 20014

HQ USAF/SGPT
Bolling Air Force Base
Washington, DC 20332-61888

HQ USAF/SGHR
Bolling Air Force Base
Washington, DC 20332-61888

HQ AFSC/XTH
Andrews AFB, MD 20334-5000

HQ HSD/CC-XA
Brooks AFB, TX 78235-5000

Department of the Navy
Naval Sea Systems Command
ATTN: Code 55X25/Mr. Pete Jung
Washington, DC 20362-5101

Defense Technical Information
Center
ATTN: DTIC-DDA
Alexandria, VA 22314-6145

HQ EUCOM
Office of the Command Surgeon
ATTN: Chief Operations/Logistics
Division
APO New York 09128

DEVELOPMENT ACTIVITY ORGANIZATION